

## REMARKS

Reconsideration is respectfully requested. Amendments to claims 29, 31, 36, 38, 40, 43-44, 65-67, 69, and 76-90 have been proposed. Entry of the amendments is respectfully requested as the proposed amendments either render the claims allowable or put the claims in better form for appeal. Claim 1-28, 37, 47-64, and 70-72 have been cancelled. After entry of this amendment claims 29-36, 38-46, 65-69, and 73-94 will be pending.

### Claim Objections

The Examiner has objected to claims 36-40, 43-45, 69-70, 79-90, and 92-93 because the claims are in improper dependent form. The amendments revise the claims so as to correct the dependency.

In light of the amendments to the claims, applicants respectfully request that the Examiner withdraw the objections.

### Claim Rejections – 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 36-40, 43-45, 69-70, 79-90, and 92-94 as being indefinite for failing to particularly point out and distinctly claim the subject matter that applicants regard as their invention. Specifically, the Examiner has stated that the recitation “the recombinant nucleic acid selected from” or “the isolated nucleic acid selected from” lacks antecedent basis.

The Examiner has rejected claims 37-40, 44-45, 70, 82-90, and 93-94 as being indefinite for failing to particularly point out and distinctly claim the subject matter that applicants regard as their invention. Specifically, the Examiner has stated that the recitation “operably linked to transcriptional ...” is not clearly linked to a particular nucleic acid.

Applicants respectfully disagree with the Examiner's grounds for rejection. However, in order to facilitate prosecution in this case applicants have amended the pending claims, without prejudice or disclaimer, to address the issues raised by the Examiner.

In light of the above amendments and remarks, the applicants respectfully request that the examiner withdraw the rejections based upon 35 U.S.C. § 112, Second Paragraph.

Claim Rejections – 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 29, 31, 33-46, 65, 70, 74, 77, 80, 83, 86, 89, and 91-94 under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner has stated that the recitation "NTR biological activity" is not limited sufficiently.

Applicants respectfully disagree with the Examiner's grounds for rejection. One of ordinary skill in the art would recognize that the biological activity of an enzyme would not include use to generate antibodies or proteolytic digestion as suggested by the Examiner. However, in order to facilitate prosecution in this case applicants have amended the pending claims, without prejudice or disclaimer. The NTR biological activity recitation has been replaced with the enzymatic function of NTR.

With respect to highly stringent hybridization, the specification clearly conveys to one of skill in the art that the inventor had possession of the claimed invention. However, in order to facilitate prosecution in this case applicants have amended the pending claims, without prejudice or disclaimer. The claims as amended clearly set out the essential hybridization condition in the form of the wash condition. The USPTO has published a document providing specific examples of application of the written description – "SYNOPSIS OF APPLICATION OF WRITTEN DESCRIPTION GUIDELINES". (Available online at:

<http://www.uspto.gov/web/menu/written.pdf>). The SYNOPSIS has an example that is squarely on point. Example 9, pages 35-37, covers hybridization claims such as in the instant application. As in the example, applicants disclose a single cDNA, SEQ ID NO:10 which as amended has a defined function – reduction of thioredoxin coupled to NADPH oxidation, which is defined in the specification on page 15, lines 15-16. The example states that, “The Art indicates that hybridization techniques using a known DNA as a probe under highly stringent conditions were conventional in the art at the time of filing.” (SYNOPSIS at page 36) At the time of filing of the instant application, hybridization techniques were well known. Applicants claims are drawn to a genus of nucleic acids all of which must hybridize with SEQ ID NO:10 and must encode a protein with a specific activity just as in the Example. The Examiner has indicated that the prior art fails to teach or suggest an isolated nucleic acid of SEQ ID NO:10 just as in the Example. Applicants disclose one species that is within the scope of the claimed genus and therefore have actual reduction to practice of at least one disclosed species just as in the Example. The Example states, “a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent conditions set forth in the claim yield structurally similar DNAs. Thus, a representative number of species is disclosed, since the highly stringent hybridization conditions in combination with the coding function of the DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention.” (SYNOPSIS pages 36-37). Thus, clearly, applicants have adequately described the claimed invention and had possession of the invention as of filing the application.

The current claims have been also cover nucleic acids with 95% identity that encode an NTR with the specified NTR biological activity , the specification clearly conveys to one of skill in the art that the inventor had possession of the claimed invention. Similar to Example 9 in the SYNOPSIS, nucleic acids that are 95% identical to SEQ ID NO:10 will be structurally similar to SEQ ID NO:10. Since there is a clear structural relationship with a defined functional

relationship to the disclosed embodiment (SEQ ID NO:10), one of skill in the art would recognize that the inventors had possession of the claimed invention as of filing the application.

In both cases, the claims have clear functional language. One of skill in the art can readily determine the scope of the claims. The specification teaches a simple protocol for testing for the claimed NTR biological activity on page 44, line 36 to page 45, line 3. Thus one of skill in the art could use the test to assay for the claimed NTR biological activity and could easily verify whether the sequence hybridized under the claimed conditions or met the 95% identity threshold. Thus one of skill in the art would recognize that the inventors had possession of the invention. The sequence alignments in Figure 4 of the specification provide further guidance to one of skill in the art for areas of the protein that are likely important for function if some level of predictability were required for written description and/or enablement.

The Examiner has rejected claims 29, 31, 33-46, 65, 67, 69-70, 74, 77, 80, 83, 86, 89, and 91-94 under 35 U.S.C. § 112, first paragraph as allegedly failing to enable a nucleic acid that hybridizes under claimed conditions to SEQ ID NO:10, 25, or 26 and have some percentage sequence identity to SEQ ID NO:10, 25, or 26.

Applicants respectfully disagree with the Examiner's grounds for rejection.

To satisfy the enablement requirement, a specification must contain sufficient information regarding the claimed subject matter as to enable one of ordinary skill in the art to make and use the invention as claimed. MPEP § 2164.01. This issue is addressed by asking the question of whether one of ordinary skill in the art could make and use the invention without "undue experimentation." The factors for assessing whether undue experimentation is required are listed in MPEP § 2164.01(a).

With respect to hybridization, the claims now provide clear conditions. Testing hybridization under such conditions is a routine matter for one of skill in the art. Furthermore, as indicated in Example 9 of the SYNOPSIS discussed above: "a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent conditions set forth in the claim yield structurally similar DNAs." Thus, the

claims are not drawn to a broad range of nucleic acids. The claims are further limited by the requirement that the protein encoded must have the claimed NTR biological activity. Testing the protein expressed from the gene for such activity requires only routine screening of the protein for its ability to catalytically reduce thioredoxin coupled to NADPH oxidation. As discussed above, the specification provides a routine test for such activity. Thus, the scope of the claims is not unduly broad and the experiments required are all routine.

Furthermore, the skill in the art is high. Such work is performed by scientists at a graduate or post-doctoral level. The state of the prior art is advanced. As mentioned above, testing hybridization is a routine matter in the art. In addition, as of filing the application, transformation of plants was well developed. Expressing a gene in any particular plant is fairly predictable. The Examiner has suggested that the unpredictability of what the exact sequences that will have the claimed function renders the claims not enabled. This cannot be the standard by which enablement is determined. The legal standard for enablement cannot be that one of skill in the art can predict the exact sequences that will or will not provide the claimed function. By way of analogy, claims to antibodies that bind to a given protein are well established as allowable where the protein is novel, but no one of ordinary skill in the art can predict the sequence of even one antibody, much less every possible antibody that could bind to the protein. Rather such claims are considered enabled, because the routine protocols of immunization, generation of monoclonals, and screening such monoclonals for their ability to bind to the given protein are in theory sufficient to generate every possible antibody and therefore enable one of skill in the art to make and use the invention commensurate in scope with the claims. Similarly, with the claimed invention in the present application, routine protocols available would enable one of skill in the art to isolate nucleic acids that bind to SEQ ID NO:10 under the claimed stringency conditions or have 95% identity to SEQ ID NO:10 and then screen the protein encoded by such nucleic acids for NTR biological activity. These routine protocols are sufficient to allow one of ordinary skill in the art to make and use the claimed invention commensurate in scope with the claims. It is irrelevant that one of skill in the art could not predict with 100%

accuracy which sequences will have the claimed function otherwise claims to antibodies would not be allowable because one of skill in the art could not predict with 100% accuracy which antibody sequences would bind to a given protein.

The Examiner has asserted that the ability to claim antibodies that bind to a particular antigen is not germane to the situation because the present claims are not to antibodies. The fact that the claims are to a different type of protein gene does not render the analogy meaningless. The analogy clearly demonstrates that the legal standard for enablement that the Examiner is applying with respect to predictability of the sequences covered by the claims cannot be correct. If the legal standard for such predictability were correct, then no such claims to antibodies would be allowable given that one of skill in the art cannot predict the sequence of antibodies that will bind to a particular antigen.

Thus, the invention as claimed is enabled because the breadth of the claims is reasonably narrow; the state of the prior art is well developed for techniques of molecular biology, enzymology, plant transformation and gene expression; the disclosure in the instant specification provides reasonable predictability; the level of skill in the art is high; the specification provides specific working examples, and the quantity of experimentation is not undue.

Therefore, applicants respectfully request that the Examiner withdraw the enablement rejections.

#### Claim Rejections – 35 U.S.C. § 102

The Examiner has rejected claims 29, 33-35, 41-42, 46, 65, and 91 as being anticipated by Lalgudi *et al.* (US Pat. No. 6476212).

Applicants respectfully disagree with the Examiner's rejection. In order to anticipate, the reference must teach every element of the claims. The claims have been amended to clarify that the proteins encoded by the nucleic acids catalyze the reduction of thioredoxin coupled to NADPH oxidation. One of skill in the art would not believe that the fragment disclosed in

Lalgudi would have this NTR biological activity. Bob Buchanan supports this view in his declaration submitted with the last response (the Buchanan Declaration). As indicated in Buchanan Declaration, the fragment lacks the active site of the enzyme, lacks the NADPH binding motif and lacks one of the two FAD binding motifs. Without an active site, the fragment will not function. Thus, Lalgudi fails to teach a nucleic acid encoding a protein with the claimed NTR biological activity. The Examiner has asserted that being cleavable by a protease or being useful for raising antibodies constitute “NTR biological activities” without citing to any support. While no longer relevant given the amendments, the applicants still traverse this assertion to preserve their rights to challenge this assertion in later applications. The Examiner has provided no support for this assertion. Applicants are unaware of the source of such assertion. Applicants respectfully traverse this assertion and request that the Examiner provide references that demonstrate that one of ordinary skill in the art would consider use to raise antibodies or ability to be cleaved by a protease as a *biological* activity of an enzyme so that the applicants can better understand the Examiner’s argument. MPEP § 2144.03 “If the applicant traverses such an assertion the examiner should cite a reference in support of his or her position.”

#### Claim Rejections – 35 U.S.C. § 103

##### A. The Examiner’s Rejections

The Examiner has rejected claims 36-40, 43-45, 69-70, 79-90, and 92-93 under 35 U.S.C. § 103(a) as being unpatentable over Jacquot *et al.* in view of Shi *et al.* (Plant Molecular Biology 23:653-662, 1996).

##### B. The Claimed Invention

The invention as claimed includes a nucleic acid that hybridizes to SEQ ID NO:10, 26, and 27 at high stringency or a nucleic acid having at least 95% sequence identity to SEQ ID NO:10, 26, and 27 in a plant, plant cell, or plant seed.

### C. Cited References

Jacquot *et al.* teach the nucleic acid encoding the Arabidopsis NADPH-dependent thioredoxin reductase (NTR). Jacquot *et al.* teach a host cell (*E. coli*) comprising such nucleic acid and recovery of protein expressed from such nucleic acid. Jacquot *et al.* do not teach transgenic plants which comprise the NTR encoding nucleic acids or constructs. Shi *et al.* teach transgenic plants expressing recombinant thioredoxin.

### D. Cited References Distinguished

35 USC 103(a) states “a patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to person having ordinary skill in the art to which said subject matter pertains. The *prima facie* case must satisfy three requirements: 1) the references must teach or suggest all the claim limitations; 2) the prior art combined with general knowledge must include a suggestion or incentive to modify or combine the references; and 3) the modification or combination must have a reasonable chance of success.

The Examiner fails to establish a *prima facie* case for obviousness in the above rejection. Specifically, the Examiner has not cited to a motivation or suggestion to combine the cited references. The MPEP is clear that a suggestion or motivation is not just any comment that modification of a reference or combination of references could be done. See MPEP 2143.01, “The prior art must suggest the desirability of the claimed invention.” The Examiner has responded by citing that motivation can be found implicitly in the reference or from the knowledge generally available to one of skill in the art. The Examiner has stated that the motivation would be to express the protein in an alternate system. This motivation is not found in either reference either explicitly or implicitly. Jacquot *et al.* expressed the protein in *E. coli* and even indicated that the protein expression in *E. coli* was very efficient (See page 1361, col



1), but did not suggest even the general desirability of expressing the protein in any other system, much less the specific desirability of expressing the protein in plants. Shi *et al.* also fail to provide any motivation to express the NTR protein of Jacquot *et al.* in the expression system disclosed in Shi *et al.* The Examiner has not cited to any general knowledge or implicit teaching of the references that would motivate one of skill in the art to combine the references. The Examiner has asserted that one of skill in the art would use a plant expression system due to post-translational modifications of the NTR protein; however, neither Shi *et al.* nor Jacquot *et al.* suggest that there are post-translational modifications of the NTR protein that are needed for function. Jacquot *et al.* noted no known motifs for post-translational modification in the sequence and the enzyme expressed in *E. coli* showed expected levels of activity. The Examiner has provided no support for this assertion. Applicants are unaware of the source of such assertion. Applicants respectfully traverse this assertion and request that the Examiner provide references that demonstrate that at the time of filing the application, one of skill in the art would expect that the NTR protein would have post-translational modifications that would need to be so that the applicants can better understand the Examiner's argument. MPEP § 2144.03 "If the applicant traverses such an assertion the examiner should cite a reference in support of his or her position." There is simply no stated need for an alternative expression system of any kind much less the exact expression system of Shi *et al.*

In addition, the Examiner has indicated that one of ordinary skill in the art would be motivated to express the NTR in plants to study the Arabidopsis protein in plant. Again, neither Jacquot *et al.* nor Shi *et al.* suggest such an experiment for further characterization of the enzyme either explicitly or implicitly. Even if they do suggest the further characterization of the enzyme, the Examiner has selected one of a nearly limitless number of experiments that one of skill in the art might select to further characterize the enzyme. Neither reference suggests the particular experiment that the Examiner has proposed. Absent some suggestion or teaching in either Jacquot *et al.* or Shi *et al.* that it would be desirable to express the nucleic acid in plant, i.e., the claimed invention, there is no *prima facie* case of obviousness.

Applicants therefore respectfully request that the Examiner withdraw the obviousness rejection.

## CONCLUSION

In light of the above amendments and remarks, applicants submit that the pending claims are in condition for allowance. Should there be any remaining issues that remain unresolved, the Examiner is encouraged to contact the undersigned by telephone.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 416272001410. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

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